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(54) **Segmented absorbable copolymer.**

(57) A copolymer comprising a bioabsorbable, segmented molecular architecture has been invented. The copolymer has at least two different ester linkages. The segmented molecular architecture comprises a plurality of fast transesterifying linkages. The fast transesterifying linkages have a segment length distribution of greater than 1.3. The segmented molecular architecture also comprises a plurality of slow transesterifying linkages. The copolymer is useful as an article of manufacture, for example a molding resin, surgical element and controlled release device.

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This invention relates to a method of forming a bioabsorbable copolymer of specific and well defined molecular architecture, to the copolymer made by the method and to a medical or surgical device manufactured from th copolymer.

Th term "molecular architectur ," which is used in describing the present invention, refers to copolymers categorized as statistical (also called random), block or segmented (also called multi-block or random-block). Block copolymers can be diblocks, often symbolized as an AB block structure, or tirblocks, often symbolized as an AAB block structure. Other block structures known in the art are "star-block" copolymers and "graft-block" copolymers. Segmented copolymers are sometimes symbolized as an $(AB)_n$ block structure. All of these architectures are well known to those skilled in polymer science.

The use of segmented copolymers in the preparation of medical devices is well known in the prior art. Interest in these materials stems from their excellent mechanical properties, which include combinations of their elastomeric behavior, high tensile strength, low stress relaxation (creep) and resistance to long term flexural fatigue failure. The excellent mechanical properties of these copolymers can be attributed to phase separation (domain formation) of the often noncrystalline "soft" segments and often crystalline "hard" segments contained within the copolymer chain. The soft segment contributes to the elastomeric behavior of the copolymer while the hard segment non-convalently crosslinks the copolymer and adds mechanical strength and toughness.

The prior art in the field of non-absorbable polymers teaches one skilled in the art of the importance of molecular architecture in determining material physical properties. Examples of non-absorbable copolymeric materials having a segmented molecular architecture that have been used in medical applications are HYTREL™ polyester (DuPont Co., DE USA) and BIOMER™ polyurethane (Ethicon, Inc., NJ USA).

The use of cyclic ester monomers in the preparation of block copolymers is known in the art. Investigators have used low temperature polymerization methods, often in solution, and exotic catalysts to avoid transesterification reactions to obtain a variety of block copolyesters which may be absorbable. So called "living polymerization" methods, due to the need for organic solvents, are not desirable for producing medical goods, and are not advantageous for commercial scale applications. Also, these methods are not easily adaptable to the preparation of copolymers with a broad range of segment lengths within a single polymerization.

While the prior art teaches the preparation of block copolymers via a sequential route, the concept of preparing segmented copolymers from cyclic esters with control over both the average segment length and the distribution of segment lengths has not yet been addressed in the prior art. It is the object of this invention to prepare block and segmented copolymers with predictable molecular architectures having good control over the segment lengths and segment length distributions.

Such a copolymerization method results in copolymers with unexpected architectures. For example, since transesterification is known to occur in all esters, it is unexpected to prepare well defined block copolymers, that is block copolymers without the complication of transesterification reactions, of the A-B or $(A-B)_n$ type under commonly used melt copolymerization conditions. However, we have found that when ester containing monomers such as ϵ-caprolactone or trimethylene carbonate are employed in the first stage of the polymerization, well defined block copolymers are formed without the complications of reshuffling or scrambling reactions. It is to be understood that in this application the term "epsiton-caprolactone" will be described by using both the Greek letter for epsila and the arabic letter "e", either in combination with "ϵ-caprolactone". That is, in this application the terms "epsilon-caprolactone", "ϵ-caprolactone", and "e-caprolactone" are synonomous.

A second example of an unexpected result, is that addition of a minor amount of a second monomer (such as glycolide or lactide) to the ϵ-caprolactone or trimethylene carbonate in the first stage of the copolymerization followed by the addition of a 2nd stage comprised largely of the second comonomer, results in copolymers with segmented, or $(A-B)_n$, architectures with controllable and well-defined segment lengths. Such copolymers display markedly different physical properties as compared to corresponding random or block copolymers of similar composition.

Still further, by varying the polymerization time following the second stage addition, to times beyond full conversion of monomer to polymer, one can control the distribution of segment lengths. This occurs with no change in overall conversion or copolymer composition. Segment length distribution has also been found to have a marked effect on the physical and mechanical properties of the resulting copolymers. For a given composition as the segment length distribution narrows with polymerization time, properties such as melting point, and d gree of crystallinity decline, and their related physical and mechanical properti s change accordingly.

Still further, it is unexpected that increasing the concentration of monomer known to form "hard segm nts" results in copolymers with lower melting point and degree of crystallinity and greater flexibility.

However, we have found that in the segmented copolymers of this invention, such an effect has been observed.

These materials may find use as absorbable medical or surgical devices where control over mechanical properties such as strength, stiffness and toughness is needed. Specific utility as a medical or surgical device includes, but is not limited to, a surgical suture and a controlled release device. Another utility of the copolymer of this invention may be as a surgical mesh or a tubular article, for example a vascular graft.

Summary

This invention relates to new and useful multiblock or block polymers and a process for producing bioabsorbable copolymers with predictable molecular architecture having specific segment lengths and distributions of segment lengths. The process can be used to prepare block copolymers (of the AB or ABA type) or segmented (also known as multiblock or random-block) copolymers of the $(AB)_n$ type.

The process is a two (or more) stage ring opening copolymerization using two (or more) cyclic ester monomers which form linkages in the copolymer with greatly different susceptibilities to transesterification. The process can be illustrated by describing the polymerization of a pair of monomers such as ε-caprolactone, which forms slow reacting (transesterifying) caproate linkages and glycolide, which forms fast reacting glycolate linkages when conventional tin based catalysts are employed.

The first stage (Stage I) of the copolymerization consists of a statistical copolymer which has a high content of the slower transesterifying (e.g. caproate) linkages and a low content of fast reacting (e.g. glycolate) linkages. This prepolymer forms a framework of segments consisting of runs of consecutive caproate linkages with interspersed short glycolate segments. The length and distribution of these segments depends on monomer feed composition, the reactivity ratios of the monomers and the degree of transesterification that occurs in this stage of the reaction. The framework, then, consists of segments with different reactivities for transesterification.

The second stage (Stage II) of the copolymerization consists of the addition of the fast reacting (e.g. glycolide) monomer and continuing the reaction for a specified length of time. The difference in transesterification reactivities of the two segments in the prepolymer preserves the caproate segments in the final copolymer. The second stage initially forms long glycolate segments, most likely at the ends of the Stage I prepolymer. Through transesterification, glycolate linkages from the initially long Stage II glycolate segments are gradually transferred into the shorter glycolate segments in the Stage I prepolymer. The result is a more narrow distribution of glycolate segment lengths. The resulting copolymer has a distribution of glycolate segment lengths. The resulting copolymer has a segmented (or multiblock) architecture, which is determined by the Stage I prepolymer framework, the final composition and the difference in transesterification rates. The distribution of segment lengths changes as a function of time after addition of the second stage. This distribution has a marked effect on material properties. In this way a wide range of material properties can be easily achieved by varying the reaction time for the second and any subsequent stages.

This mechanism is not necessarily limited to the caprolactone-glycolide pair. It has been shown that trimethylene carbonate shows similar behavior to caprolactone when copolymerized with glycolide, and l-lactide behaves similarly to glycolide when copolymerized with trimethylene carbonate. The observed differences in transesterification rates may be due to the interaction of the linkages with the catalyst. It is reasonable to believe that any combination of a linkage having a fast transesterification rate with a linkage having a slow transesterification rate can be used to prepare specific architectures in a copolymer of those linkages.

It is understood that the catalyst type and level of catalyst employed will affect both the relative polymerization and transesterification rates of the cyclic esters of the subject of this invention. By proper choice of both catalyst type and level, copolymers with specific architectures are prepared in a controllable manner and within a reasonable period of time. Catalysts such as stannous octoate or stannous chloride dihydrate are preferred. However, other catalysts known in the prior art, such as metal salt or metal oxide coordination catalysts, are within the scope of this invention.

The type of architectures that can be made utilizing this process can be AB diblock, ABA triblock, or segmented copolymers with wide or narrow segment length distributions. Diblocks and triblocks are made using monofunctional or difunctional initiators (alcohols) in the Stage I reaction and by using only the slow transesterification rate linkage to form a Stage I homopolymer. The Stage II linkages can only transesterify within the Stage II segment, preserving the diblock or triblock architecture.

A copolymer comprising a bioabsorbable, segmented molecular architecture has been invented. The copolymer has at least two different ester linkages. The segmented molecular architecture comprises a

plurality of fast transesterifying linkages. The fast transesterifying linkages have a segment length distribution of gr ater than 1.3. The segmented molecular architecture also comprises a plurality of slow transesterifying linkages. The following proviso is a material limitation to this invention: for the fast transesterifying linkages consisting essentially of glycolate linkages and the slow transesterifying linkages selected from the group consisting of trimethylene carbonate and caproate linkages, the segment length distribution of the fast transesterifying linkages is up to 2.0 and the number average segment length of the slow transesterifying linkages is greater than 2.5 linkages per segment. The nomenclature for the various linkages which can be used in the copolymer is more fully described under the heading "Description of the Invention", below. The calculation of segment length distribution and number average segment length is fully described in Example 4, below. It is well known in the prior art that the inherent viscosity or molecular weight of a copolymer can be manipulated by the amount of initiator employed during the polymerization. For the copolymer described in this application, an inherent viscosity of greater than about 0.1 dL/g (concentration of 0.5 g/dL in a solvent, e.g. hexafluoroacetone sesquihydrate) is preferred. For an article of manufacture, e.g. a surgical suture, requiring an industry acceptable tensile (or other) strength value, an inherent viscosity of about 1.0 dL/g (0.5 g/dL in a solvent) or greater is preferred. For an article of manufacture, e.g. a controlled release device, where a strength value is not required, the copolymer can have an inherent viscosity of lower than about 1.0 dL/g (0.5 g/dL in a solvent). For those monomers not exemplified or claimed in this application, to determine if they will comprise a fast or a slow transesterifying linkage, the monomer of choice can be substituted for the trimethylene carbonate monomer of Example 5, below. After conducting the test of Example 5, if the block length is equal to or greater than 30, the final glycolate weight percent is 68, and the inherent viscosity is about 1.0 dL/g, then the monomer comprises a slow transesterifying linkage. An inherent viscosity substantially less than about 1.0 dL/g means that the polymer formed is unstable at the test conditions.

In one embodiment of the copolymer the fast transesterifying linkages comprise lactate linkages. In another embodiment of the copolymer, the fast transesterifying linkages comprise glycolate linkages. In still another embodiment of the copolymer, the fast transesterifying linkages comprise lactate and glycolate linkages. In yet another embodiment of the copolymer, the slow transesterifying linkages are selected from the group consisting of trimethylene carbonate, caproate and dioxanone linkages. In a specific embodiment of the copolymer, the slow transesterifying linkages comprise trimethylene carbonate linkages. In another specific embodiment of the copolymer, the slow transesterifying linkages comprise caproate linkages.

Yet another embodiment of the copolymer is wherein the lactate linkages have a crystallinity of less than about 40 percent based on differential scanning calorimetry and a melting point of less than about 170°C. Still yet another embodiment of the copolymer is wherein the glycolate linkages have a crystallinity of less than about 30 percent based on differential scanning calorimetry and a melting point of less than about 215°C. In a more specific embodiment, the copolymer comprises a bioabsorbable, segmented molecular architecture having a plurality of lactate linkages. The segment length distribution of the lactate linkages is greater than 1.3, the crystallinity is less than about 40 percent based on differential scanning calorimetry and the melting point of the copolymer is less than about 170°C. The segmented molecular architecture also has a plurality of trimethylene carbonate linkages. As used throughout this application, the term "plurality" has a common English language definition, which essentially is: relating to or containing more than one.

An article of manufacture has also been invented. The article comprises a copolymer. The copolymer has a bioabsorbable, synthetic, segmented molecular architecture. The segmented molecular architecture comprises a plurality of fast transesterifying linkages selected from the group consisting of lactate and glycolate linkages, and mixtures thereof. The fast transesterifying linkages have a segment length distribution of greater than 1.3. The segmented molecular architecture also comprises a plurality of slow transesterifying linkages selected from the group consisting of trimethylene carbonate, caproate and dioxanone linkages. The following proviso is a material limitation to this invention: for the fast transesterifying linkages predominately comprising glycolate linkages and the slow transesterifying linkages selected from the group consisting of trimethylene carbonate and caproate linkages, the segment length distribution of the fast transesterifying linkages is up to 2.0 and the number average segment length of the slow transesterifying linkages is greater than 2.5 linkages per segment.

In one embodiment of the article, the fast transesterifying linkages comprise lactate linkages. In another embodiment of the article, the fast transesterifying linkages comprise glycolate linkages. In still another embodiment of the article, the fast transesterifying linkages comprise lactate and glycolate linkages. In yet another embodiment of the article, the slow transesterifying linkages are selected from the group consisting of trimethylene carbonate and caproate linkages.

In one embodiment, the article of manufacture comprises a molding resin. The molding resin compris s

th copolymer. In anoth r embodim nt, the articl comprises one or more extrusion pellets. In an alternative embodiment, the article comprises an extrusion resin. The extrusion pellets or resin comprises the copolymer. In yet another embodiment, the article comprises a film. The film comprises the copolymer.

The molding resin comprising the copolymer described in this application can be useful in a variety of industrial processes, e.g. blow, transfer or injection molding. Examples of products which can be manufactured from the molding resin described in this application include, but are not limited to, disposable eating implements and utensils, such as a plate and fork, respectively; disposable packaging, such as for fast food restaurants; and disposable containers, such as a bottle or a syringe.

The extrusion pellets or resin comprising the copolymer described in this application can be useful in a variety of industrial processes, e.g. dry spinning, and wet spinning including gel spinning. Examples of products which can be manufactured from the extrusion pellets or resin described in this application include, but are not limited to, a fiber, a film, and tubing including a porous hollow tube. The film can be useful in a variety of packaging materials.

In one other embodiment, the article of manufacture comprises a sterile surgical element. The sterile surgical element comprises the copolymer. For a general disclosure of medical (which includes the term "surgical") uses, see columns 4 and 5 in U.S. patent 4,135,622 issued January 23, 1979, which is incorporated herein by reference. It is to be understood that in this application the terms "surgical" and "medical" are essentially synonomous, unless the description in this application is clearly limited to only one of these terms.

In a specific embodiment of the article, the sterile surgical element comprises at least one filament. The filament has a Young's modulus of from about 100,000 to 700,000 psi. In another specific embodiment, the article comprises a monofilament. In a more specific embodiment, the article comprises a suture or ligature. In a most specific embodiment, the article comprises a suture or ligature having a diameter of from about 0.02 to 0.70 mm; a Young's modulus of less than about 500,000 psi; a tensile strength of from about 50,000 to 150,000 psi; and an elongation to break of less than about 50 percent.

In yet another embodiment, the article comprises a controlled release device. The controlled release device comprises the copolymer. Examples of products which can be manufactured from the controlled release device include, but are not limited to, consumer products such as for personal hygiene. Examples of a personal hygiene product can be an antiperspirant formulation, or an odor control product. In a specific embodiment, the controlled release device comprises a plurality of microspheres. The microspheres of the invention can be dispersed in a pharmaceutically and pharmacologically acceptable liquid to obtain a slow release composition for parenteral administration.

In another specific embodiment, the article comprises a controlled release device in combination with a pharmaceutically or agronomically active ingredient. It is to be understood that the term "pharmaceutically active ingredient" is generic and includes both organically synthesized drugs and medicine, and genetically engineered materials. Examples of organically synthesized drugs and medicines can include, but are not limited to, a steroid, anticancer drug, cardiovascular medication, and an antibiotic. The agronomically active ingredient includes, but is not limited to, compositions of matter, and formulations thereof, which are useful to control parasites, such as parasitic moxidectin, and as a pesticide. To control parasites, the controlled release device in combination with the active ingredient, (for example parastiic moxidectin, provides a one dose treatment method for ruminant animals whereby said treated animals are protected for an extended period against infestation by nematodes, endoparasitic insects, ectoparasitic insects acarids and ruminant pastures are protected against contamination by the infective stages of these parasites that infest said animals. The controlled release device in combination with the active ingredient also provides a method for protecting ruminant animals for a prolonged period of time against infestation by nematodes, endo-and ectoparasitic insects and acarids, and decontaminating pastures to eliminate the infective stages of said parasites by orally administering to said ruminants a bolus, as described above, which continuously releases into the rumen of the treated animals, for a prolonged period of time, a therapeutically or prophylactically effective amount of the active ingredient, such as, for example, LL-F28249α, 23-(O-methyloxime) LL-F28249α or a derivative thereof. Pesticidal compositions and processes for the preparation thereof are also within the scope of this invention. Each of the compositions contain a pesticidal agent, either alone or in a formulation, in combination with the copolymer described in this application. These compositions can provide an agronomically useful product which is characterized by extended residual activity (effectiv ness).

In y t another specific mbodiment, th articl comprises a controlled r leas device in combination with a polypeptide or protein.

Biologically activ prot ins, peptid s and polypeptid s suitable for administration in the compositions of the invention include growth hormones, somatomedins, growth factors, and other biologically active

fragments and derivatives thereof. Preferred proteins include bovine, ovine, quine, porcin , avian, and human growth hormones; and is m ant to encompass those which ar of natural, synthetic, recombinant or biosynthetic origin. Examples of growth factors include a platlet-d rived (alpha and beta), fibroblast, transforming, and insulin-like growth factor. Other proteins within the scope of this invention are cytokines, such as interferons, interleukins, various colony stimulating factors, and tumor necrosis factors. A specific embodiment of this invention is the incorporation of the biologically active protein peptide or polypeptide in the controlled release device comprising a plurality of microspheres.

In still another embodiment, the article may comprise a surgical prosthetic device, such as a fracture fixation device. The fracture fixation device can be selected from the group consisting of a bone plate, bone pin, bone rod and bone screw.

A process for manufacturing a copolymer having a bioabsorbable segmented molecular architecture has also been invented. The process comprises employing sequential addition of at least two different cyclic ester monomers in at least two stages. The first cyclic ester monomer is selected from the group consisting of carbonates and lactones, and mixtures thereof. The second cyclic ester monomer is selected from the group consisting of lactides and mixtures thereof. The sequential addition comprises:

I. first polymerizing in a first stage at least the first cyclic ester monomer in the presence of a catalyst at a temperature of from about 160 to 220°C. to obtain a first polymer melt;

II. adding at least the second cyclic ester monomer to the first polymer melt; and

III. second copolymerizing in a second stage the first polymer melt with at least the second cyclic ester monomer to obtain a second copolymer melt.

The process also comprises transesterifying the second copolymer melt for up to about 5 hours at a temperature of greater than about 180° Centigrade.

In one embodiment of the process, the employing substep I comprises first polymerizing in the first stage from about 80 mole percent of said first cyclic ester monomer. The remaining mole percentage, if any, comprises the second cyclic ester monomer. In another embodiment of the process, the employing substep I comprises first polymerizing in the first stage up to about 90 mole percent of the first cyclic ester monomer. In still another embodiment of the process, the employing substep II comprises adding more than about 80 mole percent of the second cyclic ester monomer. The remaining mole percentage, if any comprises the first cyclic ester monomer. In a specific embodiment of the process, the employing substep II comprises adding 100 mole percent of the second cyclic ester monomer.

Another process for manufacturing a copolymer having a bioabsorbable, segmented molecular architecture has been invented. The other process comprises employing sequential addition of at least two different cyclic ester monomers in three stages. The first cyclic ester monomer is selected from the group consisting of carbonates and lactones, and mixtures thereof. The second cyclic ester monomer is selected from the group consisting of lactides and mixtures thereof. The sequential addition comprises:

I. first polymerizing in a first stage at least the first cyclic ester monomer in the presence of a catalyst at a temperature of from about 160 to 220°C. to obtain a first polymer melt;

II. first adding at least the second cyclic ester monomer to the first polymer melt;

III. second copolymerizing in a second stage the first polymer melt with at least the second cyclic ester monomer to obtain a second copolymer melt;

IV. second adding at least the second cyclic ester monomer to the second copolymer melt; and

V. third copolymerizing in a third stage the second copolymer melt with at least the second cyclic ester monomer to obtain a third copolymer melt.

The process also comprises transesterifying the third copolymer melt from up to about 5 hours at a temperature of greater than about 180° Centigrade.

In one embodiment of the process, the employing substep I comprises first polymerizing in the first stage from about 80 mole percent of the first cyclic ester monomer. The remaining mole percentage, if any, comprises the second cyclic ester monomer. In another embodiment of the process, the employing substep I comprises first polymerizing in the first stage up to about 90 mole percent of the first cyclic ester monomer. In still another embodiment of the process, the employing substeps II and/or IV comprise adding more than about 80 mole percent of the second cyclic ester monomer. The remaining mole percentage, if any, comprises the first cyclic ester monomer. In a specific embodiment of the process, the employing substeps II and/or IV comprise adding 100 mole percent of the second cyclic ester monomer.

In yet another embodiment of the process, th employing step comprises polymerizing in the presence of a metal coordination catalyst. In still yet another embodiment of the process, th employing step comprises polymerizing in the presence of an initiator. In a specific embodiment of th process, the initiator is selected from the group consisting of a monofunctional and polyfunctional alcohol.

Drawings

Figure 1 shows in graphical form the various segment lengths as a function of polym rization time (after the stage III addition) for the copolymers of Examples 8B to 8I;

Figure 2 shows in graphical form the melting points for the copolymers of Examples 8D to 8I, as a function of polymerization time, after the stage III addition;

Figure 3 shows in graphical form the correlation between melting point and Lg_w for the copolymers of Examples 8D to 8I;

Figure 4 shows in graphical form the various segment lengths as a function of polymerization time (after the stage II addition) for the copolymers of Examples 9B to 9H;

Figure 5 shows in graphical form a comparison of the weighted average glycolate segment length (Lg_w) for the copolymers of Examples 8 and 9;

Figure 6 shows in graphical form the melting point as a function of polymerization time (after the stage II addition) for the copolymers of Example 9C to 9H;

Figure 7 shows in graphical form the correlation between melting point and Lg_w for the copolymers of Examples 9C to 9H;

Figure 8 shows the comparison of the average glycolate segment lengths (Lg_n and Lg_w) for the copolymers of Examples 9 and 10;

Figure 9 shows in graphical form the various segment length values as a function of polymerization time, after the stage II addition, for the copolymers of Example 11;

Figure 10 shows in graphical form a comparison of the value of the weighted average glycolate segment length, Lg_w, for the copolymers of Examples 11, 12 and 13 as a function of polymerization time, after the stage II addition;

Figure 11 shows in graphical form the relationship between melting point and the various glycolate segment lengths for the copolymer of Example 11;

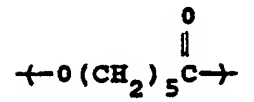
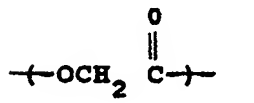
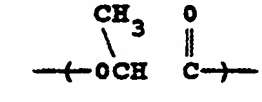
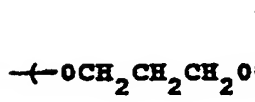
Figure 12 shows in graphical form the correlation between tensile modulus and degree of crystallinity for the copolymers of Examples 14 to 19; and

Figure 13 shows two differential scanning calorimetry traces for the copolymers of Examples 19A and 19B.

Description

It has now been found that sequential addition copolymerization of cyclic ester monomers can be utilized in conjunction with a selective transesterification phenomenon to create bioabsorbable copolymer molecules with specific architectures. Such architectures can include block copolymers (of the AB or ABA type) or segmented (also known as multi-block or random-block) copolymers of the $(AB)_n$ type.

The sequential addition polymerization process of this invention is a two (or more) stage ring opening copolymerization using two (or more) cyclic ester monomers which form linkages in the copolymer with greatly different susceptibilities towards transesterification (a phenomenon we have termed "selective transesterification"). For example, such a pair of monomers is ϵ-caprolactone which forms slow reacting (transesterifying) caproate linkages and glycolide which forms fast reacting glycolate linkages when conventional tin catalysts are employed. Nomenclature and corresponding structures of a few relevant linkages are shown below.

Linkag Nomenclature	Structure	Relativ trans ster- ification rate	Monomer
Caproate		slow	ε-caprolactone
Glycolate		fast	glycolide
Lactate		fast	lactide (d-, l-, dl-, and meso-, and mixtures thereof)
Trimethylene carbonate		slow	trimethylene carbonate

Other parent monomers which may be useful in this process include: p-dioxanone, dioxepanone, delta-valerolactone, beta-butyrolactone, ε-decalactone, 2,5-diketomorpholine, pivalolactone, alpha, alpha-diethyl-propiolactone, 6,8-dioxabicyclo octane-7-one, ethylene carbonate, ethylene oxalate, 3-methyl-1,4-dioxane-2,5-dione, 3,3-dimethyl 1,4-dioxane-2,5-dione, substituted glycolides, substituted lactides. Other cyclic esters described in the art can also be employed within the scope of this invention. These monomers may be categorizable as to their susceptibility towards transesterification. Although not specifically exemplified, such a categorization would fit within the scope of this invention.

The first stage (Stage I) of the copolymerization consists of a statistical copolymer which has a high content of the slower transesterifying (e.g., caproate) linkages and a low content of fast reacting (e.g., glycolate) linkages. This prepolymer forms a framework of segments consisting of runs of consecutive caproate linkages with interspersed short glycolate segments. The length and distribution of these segments depends on monomer feed composition, the reactivity ratios of the monomers and the degree of transesterification that occurs in this stage of the reaction. This framework, then, consists of segments with different reactivities for transesterification.

The second stage (stage II) of the copolymerization consists of the addition of the faster reacting monomer (e.g. glycolide) and continuation of the reaction for a specified length of time. The difference in transesterification reactivities of the two segments in the prepolymer preserves the caproate segments in the final copolymer. The second stage initially forms long glycolate segments, most likely at the ends of the Stage I prepolymer. Through transesterification, glycolate linkages from the initially long Stage II glycolate segments are gradually transferred into the shorter glycolate segments in the Stage I prepolymer. The result is a more narrow distribution of glycolate segment lengths. The resulting copolymer has a segmented architecture, which is determined by the Stage I prepolymer framework, the final composition and the difference in transesterification rates. The distribution of segment lengths changes as a function of time after addition of the second stage. This distribution has a marked effect on material properties. In this way a wide range of material properties can be easily achieved by varying the reaction time for the second and subsequent stages.

This mechanism is not necessarily limited to the caprolactone-glycolide pair. It has been shown that trimethylene carbonate shows similar behavior to caprolacton when copolymerized with glycolide, and l-lactide behaves similarly to glycolide when copolymerized with trimethylene carbonate. The obs rved